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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,752	05/29/2007	Michel Prost	P/24-191 V1315	9840

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EXAMINER	
HENRY, MICHAEL C	
ART UNIT	PAPER NUMBER
1623	
MAIL DATE	DELIVERY MODE
06/10/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/598,752	PROST ET AL.	
	Examiner	Art Unit	
	MICHAEL C. HENRY	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *1-4, 7-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,6 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/11/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The following office action is a responsive to the Amendment filed, 04/29/10.

Applicant's election without traverse of Group II in the reply filed on 04/29/10 is acknowledged.

Claims 1-4 and 7-9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 04/29/10.

The amendment filed 04/29/10 affects the application 10/598,752 as follows:

1. Claims 5, 6, and 10, the invention of Group II are prosecuted by the examiner. Claims are 1-4 and 7-9 are withdrawn.
2. The responsive is contained herein below.

Claims 1-10 are pending in application

Claim Objections

Claim 5 and 6 are objected to because of the following informalities: Claim 5 and 6 contains more than one period. Also, claim 6 does not end with a period. However, each claim should begin with a capital letter and end with a period. Periods may not be used elsewhere in the claims except for abbreviations. See Fressola v. Manbeck, 36 USPQ2d 1211 (D.D.C. 1995). Appropriate correction is required. Furthermore, claim 6 recites the term "formula Iib" which appears to be a typographical error. It appears that the term "formula Iib" should be replaced by the term "formula IIb". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 recites the term the phrase "especially oral or injectable excipient" renders the claim indefinite because it is unclear whether the limitations following the phrase “especially” are part of the claimed invention. See MPEP § 2173.05(d). Claim 10 recites the term the phrase "especially against chronic myeloid leukemia" renders the claim indefinite because it is unclear whether the limitations following the phrase “especially” are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition for the treatment of multiple sclerosis, does not reasonably provide enablement an immunomodulatory active ingredient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8

USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a composition which is an immunomodulatory active ingredient.

The relative skill of those in the art: The relative skill of those in the art is high.

The breadth of the claims: The instant claims are deemed very broad since these claims reads on a composition which can have immunomodulatory effects (which encompasses or includes treating numerous conditions or diseases involving, altering and regulating numerous immune functions, initiating several adjustments in the level of an immune response, and having the effect of being an Immunosuppressant as well as an immunostimulant) when administered to a subject or individual.

Regarding the Wands factor (4) the predictability or unpredictability of the art:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the recitation encompasses a

composition that can treat (for example) autoimmune diseases, which are known to be involved various, many possible, different, separate and independent, even unknown pathology, etiologies, or symptoms. The method for the treatment of an autoimmune disease is not one but at least two distinct, separate, and independent methods. For example, as defined by Ninham et at. (WO 85/05031, PTO-892), the immune response in a human or animal subject can be suppression or enhancement (see page 1-2). Autoimmune diseases can be treated by artificial suppression (immunosuppression) or enhancement (immunopotentation), wherein these two treatments are involved in distinct and separate agents, processes and mechanisms, and most importantly which are in both opposite directions.

"To date, immunosuppressive drugs that have been developed to manipulate the immune response, are usually compounds of complex structure that have been discovered by accident. Further, their mode of action is often unknown or very unpredictable and administration of drugs can be accompanied by undesirable side-effects" (emphasis added). See page 2, in particular line 19-25.

The skilled artisan would view that, treating diseases such as any autoimmune diseases, as encompassing both suppression (immunosuppression) and enhancement (immunopotentation), by administering the VERY same the composition, is highly unpredictable. Therefore, the skilled artisan would view that a composition for the treatment of disease such as the treatment of all autoimmune diseases by administering the same composition herein, is highly unpredictable.

In regard to these *Wands* factors, (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary:

In the instant case, no working examples are presented in the specification as filed showing how to treat a single autoimmune disease, i.e., no testing results provided.

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the broad treatment of any autoimmune diseases encompassed by the instant claims. As a result, necessitating one of skill to perform an exhaustive search and undue experimentation for the embodiments of treating any autoimmune diseases recited in the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation*, with no assurance of success.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for a composition or compound of formula IV for treating chronic myeloid leukemia, it does not reasonably provide enablement for a composition or compound of formula IV for treating all types of cancers.

For example, the composition or compound for treating all or any cancer or tumor cell growth, would reasonably broadly encompass those known and unknown tumors as of the instant filing date, as well as those future known cancers yet to be discovered and diagnosed.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a composition or compound of formula 1V for treating all types of cancers, which encompasses the treatment of numerous cancer or tumors.

1. The state of the prior art: The skilled artisan would view tumors as a group of maladies (cancers) not treatable with one medicament or therapeutic regimen. Treatment efforts and efforts to cure all tumors (cancers) have produced only isolated identifiable positive results. See *In re Application of Hozumi et al.*, 226 USPQ 353. Moreover, it is well known that so far no single chemotherapeutic agent has been found to be useful in the treatment of **all** cancers, or even useful in the treatment of all types of breast cancers; and colon cancers; and prostate cancers; and leukemias. For example, breast cancers and leukemia do not share a common cause and differ in their methods of treatment, i.e., breast cancers are routinely with estrogens, antiestrogens, and/or androgens, unlike leukemia which is routinely treated with I-asparaginase, daunorubicin, and purine analogs.

2. The predictability of the art, and the breadth of the claims: Note that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Moreover, it is known that repeated therapeutic failures, after promising in-vitro test results, suggest to the skilled artisan that claims based on in-vitro data, directed to treating cancer generally, are highly unpredictable, as taught in Trisha Gura's article in *Science*, November, 1997 (PTO-892):

"[T]he institute started by pulling together mouse models of three tumors: a leukemia, which affects blood cells; a sarcoma, which arise in bone, muscle, or connective tissue; and carcinoma, the most common cells and includes such major killers as breast, colon, and lung cancers. Initially, many of the agents tested in these models appeared to do well. However, most worked against blood cancers such as leukemia and lymphoma, as opposed to the more common solid tumors. And when tested in human cancer patients, most of these compounds failed to live up to their early promise." (emphasis added, see for example, the middle column of the article).

Based on the known teachings of the cancer treatment such as in Trisha Gura's reference, one of skill in the art would recognize that it is highly unpredictable in regard to the treatment in the instant case, including treating numerous and various tumors: gynacological tumors, ovarian carcinomas, testicle tumors, prostate carcinomas, skin cancer, kidney cancer, bladder tumors, esophagus carcinomas, stomach cancer, rectal carcinomas, pancreas carcinomas, thyroid cancer, adrenal tumors, various types of leukemia and lymphomas, Hodgkin's disease, tumor illnesses of the CNS, soft-tissue sarcomas, bone sarcomas, benign and malignant mesotheliomas, especially intestine cancer, liver cancer, breast cancer, bronchial and lung carcinomas, melanomas, acute

and chronic leukemias and benign papillomatosis tumors, by administering the very same composition.

4. The presence or absence of working examples: It is noted that the specification provides no working examples to demonstrate the anti-caner effect of said composition or compound on cancer in said subject. That is, the evidence in the examples provided is not commensurate in scope with the claimed invention and does not demonstrate criticality of the treatment of the numerous conditions or diseases such as tumors or cancers that are encompassed by applicant's claimed method of orally administering the said composition to subject. See MPEP § 716.02(d).

Further, those unknown or future known tumors must require additional or future research to discover and diagnose. Therefore, the skilled artisan has to exercise undue experimentation to practice the instant invention.

Thus, the specification fails to provide sufficient support of the broad use of the compounds for treating numerous and various conditions such as tumors or cancers that ere encompassed by the instant claim. As a result, there is a necessitation for one of skill to perform an exhaustive search for the embodiments involving the compound or composition and cancers encompassed by the instant claims suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factor and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test compounds or compositions and cancers or tumors encompassed in the instant claims, with no assurance of success.

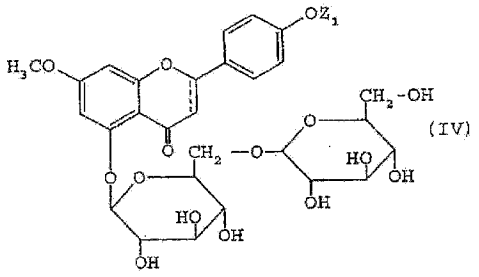
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kojo et al. (EP 0633022 A2).

Claim 5 is drawn to a saccharide derivative of genkwanin or of sakuranetin of a given general formula IV:



in which the symbol --- represents a single or double bond and Z_1 represents H or a C_1-C_4, C_1-C_5 acyl, saccharide or sulfate group and is advantageously a C_1-C_4 alkyl group or a sulfate group, and mixtures thereof.

Kojo et al. disclose a chondroprotective agent comprising a flavonoid compound of a given the general formula (I) (see abstract and claims). Furthermore, Kojo et al. disclose that the compound of general formula (I) can have a naturally occurring glycoside (see abstract and claims). In addition, Kojo et al. disclose a flavonoid compound (sakuranin) of the general formula (I) wherein Z_1 is H and which has a naturally occurring glycoside (O-glucose residue) (see abstract, claims and page 5, compound 40, sakuranin).

The difference between applicant's claimed compound and the compound of Kojo et al. is that applicant type of glycoside. That is, applicant's compound contains a naturally occurring glycoside that is an isomaltose (more specifically a two glucose residues) whereas Kojo et al.'s compound contains a naturally occurring glycoside that is a glucose (O-glucose residue). However, Kojo et al. disclose that the compounds can have a naturally occurring glycoside (see abstract and claims).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have prepared any compound taught by Kojo et al., in order to use them as chondroprotective agents.

One having ordinary skill in the art would have been motivated, to prepare any compound taught by Kojo et al. with a reasonable expectation that the compounds would have the same utility as a whole. Therefore one skilled in the art would have been motivated to make specific compounds compound taught by of Kojo et al., in order to use them as

chondroprotective agents. It should be noted that claim 10 which is drawn to atherapeutic composition contains, in combination with a physiologically acceptable and especially oral or injectable excipient, at least one compound of formula IV claim 1 is also encompassed by this rejection since it is obvious to prepare a formulation or a composition comprising the compound taught by of Kojo et al. (i.e., compound of formula IV) with a physiologically acceptable excipient in order to use it as a chondroprotective agent. It should be noted that the preparation of different formulations comprising active ingredients are common in the art and is well with the purview of a skilled artisan

Claim 10 is drawn to a cosmetic (a), dermatopharmaceutical (b) or therapeutic (c) composition, characterized in that: (a) the cosmetic composition contains, in combination with a physiologically acceptable topical excipient, at least one compound of formula I; (b) the dermatopharmaceutical composition contains, in combination with a physiologically acceptable and especially topical excipient, at least one compound of formula I; or (c) the therapeutic composition contains, in combination with a physiologically acceptable and especially oral or injectable excipient, at least one compound of formula IV as immunomodulatory active ingredient, especially against recent bouts of multiple sclerosis, or an anticancer active ingredient, especially against chronic myeloid leukemia.

Kojo et al. disclose a chondroprotective agent comprising a flavonoid compound of a given the general formula (I) (see abstract and claims). Furthermore, Kojo et al. disclose applicant's compound formula I (sakuranin) wherein Z_1 is H and R is H (see abstract, claims and page 5, compound 40, sakuranin).

The difference between applicant's claimed composition and the compound or composition of Kojo et al. is that applicant composition also comprises an exciptient.

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have prepared a composition comprising Kojo et al.'s, compound and an excipient in order to use it as chondroprotective agents.

One having ordinary skill in the art would have been motivated, to prepare a composition comprising Kojo et al.'s, compound and an excipient in order to use it as chondroprotective agents. It should be noted that the preparation of different formulations comprising active ingredients such as Kojo et al.'s compound are common in the art and is well with the purview of a skilled artisan.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry
May 30, 2010.

/Shaojia Anna Jiang/
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Art Unit 1623